

REMARKS/ARGUMENTS

Claims 1-15 were pending in the instant application. The following remarks are believed to be fully responsive to the Office Action.

THE REJECTIONS UNDER 35 U.S.C. § 103

SHOULD BE WITHDRAWN

Claims 1-15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Griffiths et al., WO03/059397 (“Griffiths”) in view of Yngve, Int. Diss. Abs. 2001, 62 (“Yngve”) and Bottcher et al., US 5,439,863 (“Bottcher”) in further view of Maier-Borst et al., GB2056471A (“Maier-Borst”). In response, Applicants submit that each of the rejections should be withdrawn for the reasons stated below.

Applicants respectively submit that Griffiths does not disclose the preparation of the agents via microwave acceleration and an anion exchanger comprising quaternary amine functional groups, polystyrene-divinylbenzene and HCO_3^- as counterions. Applicants further submit that in the Office Action, three different classes of chemical reactions having different driving forces and mechanisms were mixed up:

- Halogenation chemistry(halogenation is a chemical reaction that replaces a hydrogen atom (F, Cl, Br, I) with a halogen atom.
- Coordination chemistry (The chemistry of complex compounds made up of a metal ion and surrounded by ligands)

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- Bioconjugate chemistry (Bioconjugation involves the linking of two or more molecules, with a release of a small molecule like water, to form a novel molecule having the combined properties of its individual components.)

Yngve in her dissertation used microwave heating to carry out the conjugation reaction which does not involve ^{76}Br (coupling a prosthetic group to a macromolecule). She did not use the microwave heating to carry out the coordination chemistry (complexation of gallium by chelates). She did not even use it for the halogenation chemistry when the ^{76}Br itself was involved in the reaction (oxidative bromination). The fact that Yngve herself did not use the microwave heating when conducting her coordination chemistry using Ga clearly shows that the usage of the microwave technique for that class of chemical reactions was absolutely not obvious.

Bottcher concerns inorganic chemistry of salts and not coordination chemistry of the instant invention. Moreover, the instant invention deals with macromolecular bioconjugates. Applicants respectively submit that it is again due to a confusion of classes of reactions and compounds and terminology. Bottcher studies transition metals with diketones, dithiocarbamide acid derivatives, dihydroxy compounds, diamines or other difunctional ligands in order to use them as catalysts for polymerization and curing reactions. The instant invention focuses on Group 13 element, Ga(III) complexation with macrocyclic chelators naked or conjugated to macromolecules like peptides, oligonucleotides ect in order to improve the radiopharmaceutical production. Thus, Bottcher is not applicable to the instant invention.

The aim of the work by Maier-Borst was to synthesize an anion exchange resin for the separation of gallium-68 from germanium-68 avoiding the use of EDTA for elution as it was done before 1980s. Its aim does not collide with the claims 1-19 and the comparison is not relevant. In the instant invention, gallium-68 is eluted from a commercial generator already in ionic form. In particular the claims 1-19 consider: i) The preconcentration of gallium-68 which is needed for the efficiency of the labeling complexing reaction. Namely, the specific radioactivity for the chelator conjugated peptide labeling was increased 200-fold. ii) The volume was decreased 30 – fold, namely, from 6 mL to 200 μ L. This makes 30 – fold increase in peptide or any other macromolecule concentration. iii) The chelating ^{68}Ga -labeling reactions are sensitive to the presence of competing metal ions therefore it is important to purify the $^{68}\text{Ge}/^{68}\text{Ga}$ generator eluate from those elements. The ability of metal ions to form complexes with hydrochloric acid differs. The adsorbability of the negatively charged complexes of metals differs as well. Taking into account that the preconcentration procedure is based on the gallium ion ability to form GaCl_4^- complex, gallium can be purified from the competing metal ions using the anion-exchanging column.

It is therefore respectfully submitted that 35 U.S.C. 103 rejections of claims 1-15 as being unpatentable over Griffiths in view of Yngve and Bottcher in further view of Maier-Borst be withdrawn.

DOUBLE PATENTING

Claims 1, 3-7 and 15 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 8-14 of co-pending Application No. 10/552,206. In

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response, Applicants submit that claims will be amended or cancelled if the instant application is indicated to be allowable.

Further, claims 1, 3-6 and 9-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 8-13 of copending Application No. 11/358,681. In response, Applicants submit that a terminal disclaimer will be filed once the instant application is indicated to allowable.

Still further, claims 1-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 8-15, 18 and 19 of copending Application No. 10/552,206. In addition, claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 8-14 of copending Application No. 11/358,681. In response, Applicants submit that terminal disclaimers will be filed once the instant application is indicated to allowable.

CONCLUSION

In view of the amendments and remarks herein, applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

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The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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